Diseases of the Bones is so well known. In this case, the use of ivory pegs, as advised by Dieffenbach, and even wiring of the fragments, had failed to induce a cure. A case is also reported where Mr. Lawrence, after employing the immovable apparatus without success, has resorted to the seton, the case being under treatment at the last account; and amputation has more than once been performed in the Pennsylvania Hospital, after the failure of the seton in the femur. When a comparison is made between the use of a seton with confinement to bed for six months, or between the other means requiring confinement, and this, which permits free exercise of the limb in the fresh air, few will, it is thought, fail to give the preference to the treatment by *pressure and motion*, as accomplished through the artificial limbs.

PHILADELPHIA, *October*, 1854.

ART. VII.—*The Relations existing between Urea and Uric Acid.* By WILLIAM A. HAMMOND, M. D., Assistant Surgeon U. S. Army.

THE origin of urea is still somewhat undetermined, though numerous observations and experiments have been made by physiologists with the view of ascertaining the source or sources whence it is derived. That it is furnished, in part at least, from the metamorphosis of the effete nitrogenous tissues of the body is beyond doubt, and is admitted by all; but that it is also derived from the oxidation in the blood of the albuminates taken as food, without their previous conversion into tissue, is not so generally received.

Liebig, Bischoff, and others, hold that urea can have no other source than the metamorphosis of the worn-out tissues, and entirely reject the theory which ascribes its origin in part to the oxidation of the albuminates of the blood; whilst this latter view is supported by Lehmann, Frerichs, and Bidder and Schmidt, who adduce many experiments in confirmation of their opinion.

I do not intend, however, at this time, to discuss the question of the origin of urea. My object now is, to give the results of some experiments undertaken with the view of ascertaining whether the theory of Liebig, in regard to its formation from an intermediate substance (uric acid), could or could not be sustained by further investigation.

This hypothesis of Liebig, and the facts and inferences hitherto relied upon to sustain it, may be stated generally in few words. He assumes, as the groundwork of his theory, that uric acid is one of the primary products of the metamorphosis of those tissues, which, being worn out, are unable to resist the chemical action of oxygen.

The following formula shows how this conversion may be effected from the oxidation of protein, a substance entering essentially into the composition of all fibrous tissues:—

	C.	N.	H.	O.		C.	N.	H.	O.	
1 atom protein	48	6	36	14		15	6	6	9	1½ atom uric acid.
91 atoms oxygen				91	=	33			66	33 atoms carbonic acid.
								30	30	30 " water.
	48	6	36	105		48	6	36	105	

The uric acid thus formed is, according to Liebig, resolved, by further oxidation, into urea and carbonic acid, as follows:—

	C.	N.	H.	O.		C.	N.	H.	O.	
1 atom uric acid	10	4	4	6		4	4	8	4	2 atoms urea.
4 atoms water			4	4	=	6			12	6 " carbonic acid.
6 " oxygen				6						
	10	4	8	16		10	4	8	16	

According to this hypothesis, urea should be the predominant principle in the urine of all animals which lead active lives, and consequently inspire a large proportion of oxygen, more than is required for the formation of uric acid; and this latter substance, being first generated, should be converted by the surplus oxygen into urea and carbonic acid, and consequently should not be found in the urine of these animals, or, if present, should be but in small quantity.

On the other hand, in animals of sluggish habits, breathing but feebly, and consequently taking in but little oxygen, we should not expect to find urea, for uric acid would probably be the highest degree of oxidation the effete tissues or albuminates of the blood would be capable of assuming.

It also follows, from this theory, that the character of the food must exercise a very important influence in determining the formation of urea from uric acid. A non-nitrogenized diet, from containing a large proportion of carbon, should abstract oxygen in such quantity as to prevent the conversion of all the uric acid into urea, and consequently the former substance should exist in excess; whilst, from a highly-nitrogenized ingesta, the conversion ought to proceed under more favourable circumstances, and urea be found in greater abundance than would otherwise be the case.

Now, in fact, we find that these conditions do exist to a considerable extent. The urine of lions, tigers, dogs, &c., animals of active habits, inspiring a large quantity of oxygen, and eating highly-nitrogenized food, contains scarcely an appreciable amount of uric acid, though urea is found in abundance; and the urine of serpents, whose slothful disposition and sluggish respiration and circulation are well known, consists of little else than compounds of uric acid, no urea being present.

There are several other facts on record which tend to support the view of Liebig. Thus, Wöhler injected urate of potash into the veins of rabbits, and uniformly found an increase in the amount of urea eliminated by the kidneys. Dr. Frick has noticed that, in the convicts of the Maryland Penitentiary, uric acid was in excess in those who were allowed but little exercise, and that in

the same persons the quantity of urea was proportionably diminished. In those, on the contrary, who, from the nature of their occupations, underwent more muscular exertion, he found a larger amount of urea, and a corresponding diminution of uric acid. He also found that in those to whom cod-liver oil (a substance containing a large amount of carbon) was administered, the quantity of urea was diminished in proportion to the amount of oil taken. (*On Renal Affections*, p. 113.) Dr. Frick does not state, however, whether under this last condition the amount of uric acid was augmented or diminished.

In opposition to the hypothesis of Liebig, the experiments of Lehmann are to be taken into consideration. This eminent physiologist found, from observations made upon himself, that the uric acid was in excess at the same time with urea, and *vice versa*. Thus, whilst living on an animal diet, the quantity of urea daily excreted was 821.37 grains, and of uric acid 22.82 grains. On a non-nitrogenized diet, the urea amounted to 237.90 grains, and the uric acid to 11.34 grains; these substances bearing a more opposite relation to each other than should obtain, provided Liebig's theory be correct.

The fact that birds excrete no urea—their urine, like that of serpents, consisting of compounds of uric acid, whilst in their habits and physiology such a wide difference otherwise exists—is also opposed to Liebig's theory, and, in the present state of our knowledge, is absolutely irreconcilable with it.

Without, therefore, pretending to decide a point upon which there is so much conflicting testimony, but with the view of contributing towards its elucidation, I instituted the following experiments, the first series being performed upon myself:—

1. The object of the first experiment was to ascertain the normal quantities of urea and uric acid excreted by the kidneys in twenty-four hours, an average amount of food and exercise being taken.

I reckoned from 7 o'clock A. M., having first passed the urine which had accumulated in the night. During the day, I ate sixteen ounces of animal food, and twenty ounces of vegetable food, consisting of bread, potatoes, and turnips; drank twenty-two ounces of water, and eight ounces of strong coffee; walked two and a half miles, and rode about three miles on horseback; took no other exercise. The mean temperature for the day way 74° Fahrenheit. I passed thirty-one ounces and two drachms of urine, of specific gravity 1.021. The total amount of urea, as determined by Liebig's method with the nitrate of mercury, from 1,000 grains of the whole quantity of urine, was 682.09 grains. The total amount of uric acid, as determined from 1,000 grains of the whole quantity of urine, was 13.72 grains.

These, then, may be regarded as the average normal quantities of these substances excreted by the kidneys in my own person, and as standards for the ensuing experiments.

2. The object of the second experiment was to determine the influence of exercise on the secretion of urea and uric acid, the diet being as in the first experiment.

As previously, commenced at 7 o'clock A.M. During the day, ate and drank the same articles and quantities of food as in the first experiment. Walked briskly eight and a half miles, over a hilly country; rode ten miles on horseback; pitched quoits for two and a half hours; slept six hours. Mean temperature for the day 76°. Passed thirty-four ounces and one drachm of urine, of specific gravity 1.024. Quantity of urea (determined as in the first experiment) 864.97 grains; uric acid 8.21 grains; showing an increase in the amount of urea of 182.88 grains, and a diminution in the uric acid of 5.51 grains.

3. To determine the quantities of urea and uric acid excreted, the food and drink being the same as in the other experiments, but the body kept as nearly as possible at complete rest.

Commenced at 7 o'clock A. M. Immediately laid down on a sofa, and remained there continuously the ensuing twenty-four hours, with the exception of rising four times to urinate. Food and drink the same in every respect as before. Mean temperature for the day 73°. Slept nine and a half hours. Total amount of urine, twenty-four ounces and seven drachms. Specific gravity 1.018. Quantity of urea 487 grains; uric acid 24.86. A diminution of urea from the normal standard of 125.09 grains, and an increase in the quantity of uric acid of 11.14 grains.

These results may be embodied in tabular form as follows, the diet being the same in each experiment:—

	Quantity of urine.	Specific gravity.	Quantity of urea.	Quantity of uric acid.
Moderate exercise,	31 oz. 2 drms.	1.021	682.09 grs.	13.72 grs.
Increased exercise,	34 " 1 drm.	1.024	864.97 "	8.21 "
No exercise,	24 " 7 drms.	1.018	487 "	24.86 "

From the above, it is, I think, conclusively shown that exercise, while it increases the amount of urea, diminishes very materially the quantity of uric acid; and that inactivity, though it diminishes the amount of urea, exercises a contrary effect upon the uric acid. As far, then, as experiments of this nature can do so, these decidedly tend to support Liebig's doctrine. It must, however, still be admitted that there are great difficulties to be overcome before this view can be regarded as actually proved.

In further reflecting upon this subject, it occurred to me that if I could, by providing a greater supply of oxygen than ordinary, induce the formation of urea in animals in which it does not naturally exist, it would almost demonstrate conclusively that the hypothesis advanced by Liebig is correct.

I therefore procured a young blacksnake (*Coluber Constrictor*), and confined it in a large jar. It was fed, *ad libitum*, on flies, grasshoppers, and other insects. At the end of a week, I examined the solid excrement which had collected in the bottom of the jar. As I expected, it contained no urea; but, on dissolving it in warm water, and adding a few drops of hydrochloric acid

to the solution, a large quantity of uric acid was in a short time precipitated. I next fitted to the jar an air-tight stopper, through which passed a glass tube. Through this tube, I introduced, three times a day, for a week, about two hundred cubic inches of oxygen, which was retained in the jar for two hours at a time. By its influence, the snake was rendered excessively lively; his eyes sparkled, and he darted from side to side with surprising agility. This state of activity continued during the whole time the jar remained closed. When atmospheric air was admitted, he soon relapsed into his usual sluggish state. During these experiments, his food was the same as previously mentioned, and was devoured with increased voracity.

At the end of a week, I removed the excrement from the jar, and dissolved it in warm water. A drop of the filtered solution was suffered to evaporate on a glass slide. On viewing it under the microscope, I observed most beautiful crystals of urea, mingled with those of amorphous urate of ammonia. Not being willing to rely upon the crystalline form alone as a test, I submitted the remainder of the solution to chemical examination, as follows. The process employed was that recently proposed by Liebig as a modification of his method of testing for urea with the nitrate of mercury. Solutions of corrosive sublimate and bicarbonate of potash were prepared and mixed together. On adding this mixture to the solution containing the excrement of the snake, the white precipitate of urea and protoxide of mercury were immediately thrown down. This examination I regarded as showing conclusively the presence of urea, and that in no inconsiderable proportion.

From the several experiments recorded in this paper, and more especially from the last series, I consider that the theory of Liebig, accounting for the formation of urea, is probably correct. True, there are many facts difficult to account for on the supposition of its truth, and many well-founded experiments to set aside, but surely the evidence is not altogether opposed to it; and, though much still remains to be accounted for before it can be universally received, there is ground to expect that future investigations will do much towards its establishment.

It is my intention to pursue this subject further, by submitting other animals to experiment. It is only by continued investigation that correct ideas of so important and difficult a subject can be obtained.

ART. VIII.—*Amputation of the Thigh in Civil and Military Practice; The Comparative Success of Secondary Operations.* By RICHARD MCSHERRY, M.D., of Baltimore.

THE singular fatality which attends upon amputation of the thigh after gunshot wounds, is enough to restrain the hands of the surgeon wherever his patient